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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/574,687

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EXAMINER

KIM, TAEYOON

ART UNIT

PAPER NUMBER

1651

NOTIFICATION DATE

DELIVERY MODE

05/20/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/574,687	Applicant(s) MORITA ET AL.	
	Examiner Taeyoon Kim	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period **will** apply and **will** expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply **will**, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 February 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-7 and 9-18 is/are pending in the application.
- 4a) Of the above claim(s) 10-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-7,9 and 18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendment and response filed on 2/22/2010 has been received and entered into the case.

Claims 2 and 8 are canceled, claims 10-17 have been withdrawn from consideration as being drawn to non-elected subject matter, and claims 1, 3-7, 9 and 18 have been considered on the merits. All arguments have been fully considered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3-7, 9 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Georger et al. (of record) in view of Kobayashi et al. (of record) and Singhvi et al. (US 5,776,748).

Georger et al. teach a method of culturing cells such as endothelial cells on patterned surfaces (ultra-thin film; UTF) having selective adhesion formed by patterned irradiation (Abstract; Fig. 1; col. 3-4; col. 13, lines 5-8).

The UTF of Georger et al. is formed on a glass plate coated with EDA (aminosilane), and upon the irradiation, the water contact angle of EDA having 28-32° is changed to 92-94° (col. 4, line 65 through col. 5, line 2), providing cell adhesive region (EDA coated UTF region) and cell non-adhesive region (pure UTF region). Thus, this teaching meets the limitation of water contact angles being between 10 and 40°.

Since the EDA layer is coated on top of glass substrate, the limitation of first region (EDA coating; cell adhesive region) is formed on the second region (UTF; cell non-adhesive region). According to the Figure 3 of Georger et al., the pattern formed on the UTF is linear, satisfying the limitation of the first region (cell adhesive region) being linear.

The UTF of Georger et al. contains a surface layer comprising inorganic materials such as titanium oxides (col. 6, lines 38-53), and it is well known in the art that TiO_2 is a photocatalyst activated by UV irradiation according to Kobayashi et al.

Georger et al. teach that the UTF can be used as surfaces for body implants (col. 4, lines 19-21). Therefore, upon contact of UTF containing cells on cell adhesive region to the body as an implant, the cells grown on the UTF would be inherently transferred to a body/tissue of an implant recipient upon implantation, and this is considered non-enzymatic transfer of cells. The tissue of implant recipient is considered as a cell culture substrate.

Furthermore, since the cell adhesion mediated by EDA is hydrophobic interaction, it is expected that the force holding the cells on the surface of EDA is considered to be weak, and upon the contact of the cells to the surface having higher binding affinity would transfer cells from the EDA based patterned substrate to another.

Singhvi et al. teach such a transfer step of cells grown in pattern on hydrophobic/biophilic surface made of self-assembled monolayer (SAM) such as silicone elastomers including polydimethylsiloxane (PDMS) (col. 18, lines 12-37).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to try the transfer process taught by Singhvi et al. for the cells grown on EDA UTF of Georger et al. to a secondary substrate having higher affinity than the hydrophobic

interaction of the cells with EDA UTF.

In fact, the implantation of EDA UTF having cells grown on cell adhesive region of Georger et al. is considered the same procedure of transferring cells to another substrate having higher affinity to the cells on the EDA UTF. It is well known in the art that cell-cell interaction is mediated by various different mechanisms including cell adhesion molecules, carbohydrate-carbohydrate interaction, ligand-receptor interaction, etc. is well known to be much stronger than the hydrophobic interaction of Georger et al. or Singhvi et al.

With regard to the limitation in claim 9 of the widths and the distance (space widths between lines), not only Georger et al. teach the width of the first region (cell adhesive region; EDA UTF region) being 40 μm wide (col. 5, lines 2-20; Fig. 3), but also the specific sizes of each line formed on the substrate and the distance between such lines are considered to be result-effective variables. Because Georger et al. teach the use of endothelial cells and the patterning would be achieved by coating with at least one region of cell adhesion promoter with a width which corresponds to the desired outer circumference of the microvessel (col. 9, lines 56-63).

Therefore, the arrangement of the regions having cell adhesiveness and the regions cell non-adhesiveness would be optimized based on the desired purpose of the cell patterning device. The variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in sizes and distances will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955); see also

Art Unit: 1651

Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382; *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

With regard to the order of layers as disclosed in claim 5 or the orientation of layers (cell adhesiveness variation material and the photocatalyst-comprising layer facing each other) as in claim 6, these limitations are not required for the process steps claimed in claim 1. Rather these limitations are considered as optional, and do not require active steps to be carried out for the process disclosed in claim 1. Claim 1 is directed to steps of adhering cells on the patterned substrate having cell adhesive (first region) and cell non-adhesive (second region) regions, and transferring the cells from the first region to another cell culture substrate. Whether or not the patterned substrate having a specific order or orientation does not limit the claimed process.

With regard to the limitation of claim 18, according to Fig. 3A of Georger et al., there are two different types of first regions (cell adhesive region having two different widths; dark regions) and two different types of second regions (cell non-adhesive region having two different widths; white regions). Furthermore, it would have been obvious to a person of ordinary skill in the art to try two or more types of cells on multiple first regions and second regions of the substrate of Georger. This is because Georger teaches that the apparatus can be used for neuronal

or neuromuscular synapse formation having neuron and muscle cells adhered to the different areas of the promoter region (col. 9, line 64 through col. 10, line 6).

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Response to Arguments

Applicant's arguments filed 2/22/2010 have been fully considered but they are not persuasive.

Applicant alleged that Georger do not teach or suggest the step of transferring the pattern of cells formed on the UTF to a biological tissue, and the present invention does not intend to use the "cell array substrate" as an implant. Applicant argued that the cells arrayed on the UTF surface remain on that surface, which is incorporated into the recipient as an implant material, and the cells remaining on the UTF surface are not "transferred" as alleged by the Examiner.

It is acknowledged that Georger does not particularly teach or disclose "transferring" step of the cells patterned on the UTF surface. The Examiner interpreted that the teaching of Georger that UTFs are useful as surfaces for body implants (col. 4, lines 19-20) as that UTF can be coated on the surface of body implants, and thus, a person of ordinary skill in the art would layer the UTF having cells adhered on the surface of the body implants. However, even if it is considered that Georger does not teach the limitation, the OA clearly disclosed additional rationale citing Singhvi. As discussed, Singhvi teaches a transfer step, and a person of ordinary skill in the art would try to transfer the patterned cells on UTF.

With the combination of Georger and Singhvi, applicant alleged that Singhvi is directed to a device for adhering cells in a specific and predetermined position, and the transfer of cells

Art Unit: 1651

from the primary plate to the secondary plate in Singhvi is for the purpose of selecting individual cells positioned on islands of specified coordinates, and thus the transfer step of Singhvi is rendered useless where desired cells are not identifiably segregated on the islands of the primary plate. This argument is not persuasive. The teaching of Singhvi is directed to transferring step of cells grown on the primary plate to the secondary plate, and the claimed invention is directed to a step of transferring the cells on a patterned cell array substrate to a cell culture substrate. This does not require any selection of cells, and the claimed invention simply requires transferring step.

As discussed, Georger discloses that the patterned cells on UTF can be the surface of the body implant, and a person of ordinary skill in the art would recognize that the cells on UTF can be transferred since UTF, which is considered as self-assembled membrane (SAM; self-assembled film) of Singhvi can be transferred to the surface of body implant, and utilize the transfer step of Singhvi to transfer the patterned cells on UTF of Georger to the surface of the body implant.

Furthermore, Singhvi teaches the use of the disclosed method for generating surfaces for tissue culture, creation of artificial tissues for grafting or implantation, for generating artificial tissues to adhere to the surfaces of prosthetic or implantable devices (col. 21, lines 10-22). For example, Singhvi teaches patterned proteins may be transferred from the patterned plates by contacting the plates with other biophilic or bioadhesive substrate, and thus, the surfaces of prosthetic or implanted devices or tissue culture plates can be patterned with the patterned proteins. Under the same context, the patterned cells can be transferred to the surfaces of prosthetic or implanted devices or tissue culture plates, and a person of ordinary skill in the art

Art Unit: 1651

would certainly try to transfer the patterned cells on UTF of Georger to the surfaces of prosthetic or implanted devices or tissue culture plates with a reasonable expectation of success.

Applicant also alleged that the structural features disclosed in claims 5 and 6 should be considered for determining patentability of a process citing M.P.E.P. §2116. It is acknowledged that materials on which a process is carried out must be considered, and the previous OA has discussed the substrate having cell adhesiveness variation layer and a photocatalyst-comprising layer. The limitations of claim 5 and 6 are directed to the order or orientation of the layers which is considered as structural feature of the substrate, and it is considered that the order and/or orientation of the layers does not require any method step to be carried out for the claimed method. Unless there is evidence showing unexpected and surprising results from the specific orientation and/or order of the layers of the claimed substrate, the order and/or orientation of the layers in the substrate is considered optional and thus, a person of ordinary skill in the art would try any order and/or orientation of the layers.

With regard to claim 18, applicant alleged that the Examiner does not allege or show that Georger teaches “two or more types of cells” as claimed. It is acknowledged that the Examiner did not clearly address the limitation. The limitation has been addressed in this instant OA (see above).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

Art Unit: 1651

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/
Primary Examiner, Art Unit 1651